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Angiographic Patterns of Arteriosclerosis Obliterans in the Legs of Diabetics and Nondiabetics : Review of the Literature and the Recent Experience at Yale-New Haven Hospital

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ABSTRACT

Angiographic Patterns of Arteriosclerosis Obliterans
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The literature regarding angiographic patterns of arteriosclerosis obliterans (ASO) in the legs of diabetics and nondiabetics is reviewed.

The medical records of 28 adult-onset diabetics and 35 nondiabetics with chronic ASO of the lower extremities who underwent angiography for the first time were analyzed for age, presenting symptoms, smoking history, history of hypertension and therapeutic fate of the affected limbs. The arteriograms were analyzed for basic disease patterns and degree of disease at specific segments of the arterial tree, based on the radiologist's findings. Diabetics have more popliteal and trifurcation disease than nondiabetics, but less than has been found in previous studies. Nondiabetics have significantly more aortoiliac disease. The two groups present at the same average age, but with worse clinical symptoms and findings in the diabetic. The diabetic limb is typified by worse symptoms in the presence of better blood flow than the nondiabetic limb, possibly due to decreased resistance to infection and superimposed autonomic/sensory neuropathies. As a result, the diabetic undergoes more major and minor amputations. Because diabetics and nondiabetics have been seen to fare similarly with bypass surgery, it is suggested from this study that diabetic limb salvage might improve if intervention is undertaken earlier in the course of diabetic leg vessel ASO. Larger series are needed to compare and update the comparative arteriographic patterns of lower extremity ASO in diabetics and nondiabetics, and to further define the fate of the diabetic claudicator.

This thesis is lovingly dedicated to my parents,

Naomi and Henry Wahrman
and my sisters Tirza and Miriam

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I. INTRODUCTION

The third edition of Eliot P. Joslin's landmark text, The Treatment of Diabetes Mellitus, With Observations Based on Three Thousand Cases (1923) (38) is appropriately dedicated to Banting and Best, and the "Toronto Group of Insulin Workers". Nearly ecstatic in tone, the preface reads:

> Yet can the reader imagine the feeling of a doctor with a background of 1000 fatal cases, who has lived to see what the ages have longed for come true in the discovery of insulin...

Cautiously, Joslin also states that, "Insulin does not cure diabetes, but it is a priceless gift to the severe diabetic provided he is intelligent and faithful..."

Despite the hope born that year with the isolation of insulin and its later therapeutic implementation for a certain segment of juvenile- and adult- onset diabetics, other treatment modalities such as diet and hypoglycemics are used in less severe (non-ketosis prone) cases of the disease. However, many of the same complications of sixty years ago continue to haunt the diabetic of today.

Gangrene merits no less than thirteen pages in Joslin's book. It is quoted as being the cause of death in 23% of 775 cases of DM in Boston from 1895 to 1913. From Joslin's own experience, 3% of his series (up to 1923) of 2611 paients were affected, but accounted for fatalities in only 6%, and afflicted 2% of those still alive. Statistical breakdown, however, showed an incidence of of 10% for those in the seventh decade of life, and 20% in the eighth.

Joslin's discussion includes an interesting quote from Leo Buerger:

> A study of the conditions of the arteries and veins in limbs amputated for so-called diabetic gangrene reveals the fact that we are dealing not with a gangrenous process due to the diabetes per se, but a mortifying process dependent upon extensive arterial disease... In short characteristic for so-called diabetic gangrene is the presence of the typical lesions of the arteries of the arteriosclerotic or senile gangrene, and justify the conclusion that in diabetic gangrene we are dealing with an... arteriosclerotic process (38).

The implication of the word senile is that the changes of the diabetic's vessels are remarkable only in that they somehow occur earlier in life.

West pithily updates the problem six decades later:

> Gangrene is one of the most important and distressing manifestations of diabetes. It is not generally appreciated that among populations of diabetics there are very great differences in susceptibility to this dread complication. But rather little has been learned previously concerning the epidemiology of gangrene and other disorders secondary to diabetes-related peripheral vascular disease. Indeed the present status of data in this field is an epidemiologists nightmare! ...few studies have been performed in representative samples of diabetics or nondiabtics. Controls have been few and suboptimal... The relationship between diabetes and peripheral vascular disease is so strong that little need has been perceived for investigation. To most Western clinicians this suggested an inevitability of association and tended

> to stifle incentives to look for preventive measures. The most prominent and important of these manifestations of excessive leg vessel disease is gangrene but there are other morbid efects. These include intermittent claudication and pain at rest... Ulcerations of the toes and feet are often disabling. There are no counterpart to these lesions in the upper extremity. Probably "leg artery disease" would be more appropriate than peripheral vascular disease. (76)

The literature on diabetes and that on atherosclerotic peripheral vascular disease are vast and ever expanding. Whole monographs have been written on the care of the diabetic foot alone (47), and entire seminars devoted to problems of its management (77). Yet much of what is commonly known regarding the gross anatomic differences between diabetic and nondiabetic leg vessel disease is somewhat anecdotal and based on few studies. Diabetic leg vessel disease is further complicated by autonomic and sensory neuropathies (23), and by reduced ability to heal tissue ulceration and fight infection (43). The relationship between metabolic derangements and ischemic insult, whether at the level of the named arteries or at the level of the as yet theoretical "diabetic microangiopathy" (68) awaits unravelling. It is a given that proportionate to their numbers, diabetics have a much greater and accelerated incidence of atheromatous leg vessel disease, but this cannot and should not be equated with the angiopathy of the juvenile-onset patient, nor, for that matter, that of the maturity-onset diabetic, both associated with retinopathy or nephropathy (63,79). Thus, Buerger's comparison of diabetic (ASO + DM) and non-diabetic atherosclerosis (ASO) (page 2) has still not been conclusively disproved when speaking of the lower extremities. Despite the known association of diabetes and atherosclerosis, the question of the differences, if any, in the pattern of atherosclerosis between diabetics and non-diabetics remains unresolved.

It is the purpose of this paper to review the literature regarding the comparative angiographic pattern of lower extremity ASO in diabetics and nondiabetics. In addition, the recent experience at Yale-New Haven Hospital with a series of patients admitted for angiographic evaluation of ischemic lower limbs will be examined in reference to the pattern of disease, clinical presentation, risk factors and therapeutic outcome.

II. Review of the Literature

A. Angiographic Patterns of Disease

Prompted by the advent of reconstructive vascular surgery during the 1950's, and the more recent advent of transluminal angioplasty for the treatment of occlusive disease, angiography remains the most important and precise method for evaluation of arterial anatomy when surgical intervention is clinically indicated. These indications usually include: a) acute ischemic symptoms b) rapid progression of intermittent claudication or claudication that significantly interferes with employment or recreation c) rest pain d) ulcers/gangrene of the foot or leg. Although intermittent claudication secondary to arterial occlusion was once seen as a herald of future threatened limb loss, it is now recognized to remain stable or improve in 70 - 80% of nondiabetic cases and is not usually a strict indication for angiography or bypass (51,36).

Lindbom (48) and Mavor (54) provided among the first descriptive accounts of lower extremity arterial occlusive disease based on arteriographic findings. However, the work of Haimovici and associates, employing the technique of serial femoral studies, represents the first major attempts to systematically classify as well as quantify ASO in the lower extremity of the diabetic and non-diabetic.

In a 1960 paper (32) based on the femoral arteriograms of 91 patients (64 males and 27 females ranging in age from 29 to 87), intermittent claudication was the presenting complaint in 33%, rest pain in 22%, rest pain with leg or foot ulcers 17%, and frank gangrene in 28%. Of the latter two groups, 61% of the patients were overt diabetics, but overall, diabetics with ASO accounted for 36% of the patients studied, whereas non-diabetic patients with ASO accounted for 58%, and embolic phenomena and Buerger's disease accounted for the remaining 16%. The angiographic lesions of the femoral/ popliteal system were classified based on nine occlusive patterns, and their incidence in non-diabetics and diabetics noted:

PATTERN (artery occluded)	ASO (%)	ASO + DM (%)
1. Distal SFA	12.8	23.7
2. Proximal SFA	5.1	1.7
3. Entire SFA	20.4	8.5
4. Proximal popliteal	15.5	17.0
5. Distal popliteal	6.4	6.7
6. Entire popliteal	6.4	15.1
7. Entire SFA & popliteal	12.8	6.7
8. Profunda femoris	5.1	11.8
9. Diffuse changes of ASO with multiple stenotic areas	15.5	8.8
	100.0	100.0

In 68 patients a single pattern number sufficed to describe the angiogram. In 33 cases two numbers were used and in only one case was three numbers needed. For instance, among the diabetics the most common combinations were 1 + 4, 1 + 6, 1 + 8, and 3 + 4. Among the non-diabetics 3 + 4 and 7 + 8 were often seen combined. The ASO seen in diabetics accounted for 61.8% of all combined patterns.

Evaluation of the run-off below the knee was assessed only in those patients with a patent distal popliteal artery (i.e. patterns 1, 2, 3, or 4 singly or in combination), and then graded as "good, fair or poor", although the grading criteria are not given. With ASO alone, a "good" runoff was found to be be three times more likely than in ASO and DM. When the trifurcation vessels were judged for roentgenographic patency, it was also found that non-diabetics had an eight- to nine-fold patency rate of all three vessels (27.4% vs. 3.3% in diabetics). Among the diabetics there was a 1.5 greater chance of complete occlusion of the tibial-peroneal arteries (54.8% vs. 36.4% in ASO alone). The different proximal or distal pattterns were not correlated with specific clinical presentation or outcome. Of the 18 patients who underwent amputation (5 transmetatarsal, 8 below-knee, 5 above-knee), 10 were diabetics.

Gensler, Haimovici et al. (26) compared the angiographic patterns of 124 diabetics and 181 nondiabetics, the majority of whom presented with rest pain with or without breakdown of the soft tissues, or ulcers/gangrene alone.

75% of all patients had intermittent claudication as their chief complaint prior to these more advanced clinical presentations. 29% of the nondiabetics and 15% of the diabetics presented wih rest pain and no evidence of tissue breakdown. 49.2% of diabetics and 19.3% of non-diabetics presented with ulcers/gangrene. No instances of diabetic neuropathy are mentioned.

The male:female ratio in nondiabetics was 4:1 and in diabetics 1.5:1. However, below the age of 60, it was 3:1 in diabetics. 54% of diabetics and 42.5% of nondiabetics had blood pressures higher than 150/90 mm Hg.

The arteriographic patterns were presented in a more condensed fashion based on % occluded limbs:

LOCATION OF OCCLUSION(S)	ASO	ASO + DM
1.Superficial Femoral Artery	6.2	2.6
2.Popliteal	3.2	5.2
3.Tibial Arteries	0	.5
4.SFA & popliteal	16.3	1.7
5.SFA & politeal & tibials	42.6	75.4
6.Aortoiliac	6.2	1.7
7.Aortoiliac & SFA & popliteal &tibials	25.0	13.4
	100.0	100.0

The authors conclude that the difference between the two groups lies in the distribution of the vascular lesions. The diabetics have ASO which affects not cnly the major limb vessels, but "also and mostly" the medium and small arteries that represent the terminal arterial bed. Examination of the data regarding the more severe and diffuse patterns of disease, namely 5 and 7, do indicate a substantial predominance of the former pattern in the diabetic but also a nearly doubled incidence of the latter pattern in the nondiabetic, where proximal inflow as well as more distal run-off is involved. Of note is the low incidence of isolated lesions of the tibial-peroneal trunk, and the higher incidence of pattern 4 in the nondiabetic.

Of these 305 patients, 251 (82.3%) were candidates for revascularization procedures, 22 (7.2%) had primary amputations and 32 (10.5%) were treated conservatively. At a follow-up of between .5 - 8 years in 242 patients, surgical procedures (bypass, endarterectomy, sympathectomy) in patients with diffuse disease and "poor" run-off accounted for overall "good" results in 77% of nondiabetics and 54% of diabetics. Again, the criteria for quality run-off is not specified, but good results referred to relief of presenting symptoms and healing of skin lesions. Arterial surgery alone resulted in comparable "good" results in 79% of nondiabetics and 73% of diabetics. Sympathectomy alone or combined with arterial surgery yielded worse results in the diabetic patients, 53% vs. 78% in ASO alone in the former instance and 36% vs. 73% in the latter.

Unfortunately, we are not provided with a correlation of pattern, clinical presentation and management of the affected limb(s). Although both groups seem subject to involvement of the entire arterial tree, it would have been instructive to learn which patterns accounted for the similar success rates of pure revascularization.

A later more detailed study by Haimovici (30) presents the data on 321 lower limbs of 189 patients. 79 were overt and 12 were chemical diabetics. They had a similar range of presenting ischemic complaints as in the above studies. Analysis was geared towards a more comprehensive study of lesion type (i.e. intimal plaque, significant stenosis, obstruction, aneurysm), site and extent. The sites of various lesions were classified under a revised system (% limbs with the particular pattern):

LOCATION OF DISEASE	ASO	ASO + DM
1.Tibial-peroneal	23.9	29.2
2.Popliteal	5.6	1.9
3.Popliteal-tibial	12.0	18.8
4.Femoral & popliteal	9.0	1.4
5.Femoral & popliteal & tibial	19.7	24.7
6.Femoral & popliteal & tibial with aortoiliac stenosis	18.5	16.2
7.Femoral & popliteal & tibial with aortoiliac occlusion	3.0	3.9
8.Femoral & popliteal & tibial with aortoiliac aneurysm	8.3	3.9
	100.0	100.0

Pattern 1 again refers to isolated lesions of the trifurcation vessels, but involvement of these arteries was seen with just about all other proximal patterns. Further breakdown of data concerning runoff below the popliteal artery shows that in cases of isolated tibioperoneal involvement nondiabetics show only one vessel involved in 65% of cases and diabetics in 31%. Likewise, all three vessels were diseased in 12% of ASO alone and in 33% of diabetic ASO. When trifurcation lesions were combined with other proximal lesions, one vessel disease was seen in 49% of nondiabetics and 28% of diabetics, whereas more severe three vessel involement was seen in 13% of nondiabetics and 33% of diabetics.

In the 1960 paper of Haimovici et al. (32), lesions of the profunda femoris artery (PFA) were seen in 5.1% of nondiabetics and 11.8% of diabetics. The series of previous investigators had reported no incidence of PFA involvement (48,54). In the later (1967) paper just summarized, the PFA showed evidence of ASO involvement of 9.5% Of nondiabetics and 30.5% of diabetics. The PFA is a significant source of collateral circulation (e.g. the 3rd and 4th muscular branches) and its higher rate of involvement in the diseased limb of the diabetic is ascribed clinical importance by the author, because the more distal disease in these patients (about and below the trifurcation) is thus supplied by a less extensive collateral system, the genicular-tibial arterial network. In discussing the pathologic correlates of these angiographic findings, Haimovici states that the incidence of segmental, isolated lesions in patients with occlusive disease is variably estimated to be between 10 - 50% (source not given). The apparent discrepancy may be the the method of patient selection for angiography. Thus, the earlier the phase of the disease, the greater the likelihood of monosegmental occlusion, with proximal and distal lumina displaying minimal change. Accordingly, at a later stage, more diffuse changes are seen, with impending coalescence of occlusions and/or stenoses. The ASO in diabetics is typified by accelerated diffuse change with relative sparing of the aortoiliac segment (33,20). The association of aortoiliac disease with lesions distal to the inguinal ligament (especially in the nondiabetic) and the imporance of its inclusion in evaluation by serial arteriography is emphasized in another paper using the same patent cohort (33).

Hoar et al. (34) at the New England Deaconess Hospital / Joslin Clinic used Haimovici's earliest system ((22), see page 8) to characterize 294 femoral arteriograms of 117 males and 128 females, all diabetic, who presented with somewhat more advanced disease. 60% presented with gangrene/ulcers of the feet, 30% with ischemic rest pain, and 10% with rapidly advancing claudication. The system was modified with greater emphasis placed on the status of the tibial-peroneal anatomy. 'PP' designated a patent, but poor popliteal artery unsuitable for bypass grafting. Two or three patent trifurcation vessels was considered 'good' runoff, whereas only one patent vessel was considered 'fair'. A designation of 'poor' was given if all three vessels were occluded somewhere in the calf, and '0' was assigned if no vessels were seen in the proximal half of the calf. Based on the trifurcation anatomy and the filling appearance of any collateral circulation in that region, Hoar et al. formulated four basic grades of anatomy, combining proximal patterns with infra-popliteal run-off. The number of diabetic limbs in each grade is given:

Grade 1 =======	no occlusions or pattern 1,2, or 3 runoff- good; collaterals- good	(41)

Grade 2	no occlusions or pattern 1,2,3, or 8 runoff- fair; collaterals- good or fair pattern 4 runoff- good; collaterals- good or fair	(46)
Grade 3	all other patterns, all PP runoff- poor; collaterals- fair or poor	(98)
Grade 4	pattern 5,6, or 7 runoff- poor or 0	(90)

Nineteen of the arteriograms were judged to be of poor quality and thus were not graded. 98 SFA-popliteal bypasses were performed and followed for patency rates over three to eight years. Absolute successes (graft patency and alleviation of presenting symptoms) ranged from 75% in Grade 1 to 22% in Grade 4. We are not given the distribution of symptoms in each grade. Overall there were 60 absolute and 10 qualified successes; in the latter the graft occluded after the offending symptoms resolved. Of the 90 major amputations, the first two grades accounted for only 8, but accounted for 33% of the minor amputations (toes, transmetatarsal). Lumbar sympathectomy was performed in 25 instances with only 8 successes, but the anatomic grades of these patients is not indicated. Again, it is of note that 69% of these patients, all diabetic, had poor runoff below the popliteal, but based on their clinical picture in toto, they were seen at a rather advanced stage of their leg-vessel disease. Of note, is that 67% of these patients were between ages 61-80, which is much closer to the age distribution of femoropopliteal disease in nondiabetics than would be expected; for instance, in Haimovici (30), 65% of the patients, including diabetics and nondiabetics, were between ages 51-70. The mean duration of diabetes in the Joslin group was 16 years. 66% of these patients had at least one of the diabetic sequelae of retinopathy, neuropathy, or nephropathy. Obesity was noted in 53%, smoking history in 39% and EKG abnormalities noted in 70%. In 35% of these patients, death resulted within the follow up period, 26% attributable to cardiovascular disease. Interestingly, patients who had better runoff at initial study (Grades 1 and 2) accounted for 24% of the deaths at follow up whereas the more severely diseased limbs (Grades 3 and 4) accounted for 76% of the follow-up deaths; the state of the trifurcation vessels seemed here to be in rough correlation with the systemic effects of arteriosclerosis and diabetes.

In an attempt to further define the natural history of arteriosclerosis obliterans, which has as its endpoint various patterns of leg vessel disease, Rosen et al. (60) attempted to correlate three basic configurations of disease with certain risk factors. Based on physical examination and arteriography in 109 patients, the three patterns of disease were defined as aortoiliac or A (31 patients), aortoiliac-femoropopliteal disease or C (24 patients), and femoropopiteal disease or L (54 patients). The risk factors assessed were were similar to those used in the Framingham study (28):

1. History of cigarette smoking (10 or more cigarettes per day up to 6 months prior to commencing the study)
2. Hypertension (blood pressure > 150/90 mmHg)
3. Serum cholesterol > 250 mg/ 100ml
4. Serum triglycerides > 130 mg/ 100ml
5. Fasting blood sugar > 100 mg/100 ml
   2 hour post - prandial blood sugar > 120 mg/100 ml
6. Lipoprotein electrophoresis abnormalities
7. EKG abnormalities

Patients with the A pattern had the lowest incidence of glucose intolerance at 17%, significantly lower than C (50%) or L (48%). The specific number of diabetics and duration of their disease is not provided. The average age of A patients was 58 years, whereas 65 years was the average age in the other two groups. The male:female ratio was 3:1 in A, 1.4:1 in C, and 1.7:1 in L. The most common lipid abnormality in all groups was Type IV hyperlipoproteinemia (elevated triglycerides and VLDL) which affected 35% in A, 22% in C, and 52% in L, a significant difference from the other two groups. Hypertension was lowest in group L and highest in A, and EKG abnormalities were highest in C, 71% versus 55% in the other two groups, but these two risk factors did not reach significance when compared. The most prevalent risk factor in all groups was cigarette smoking, 90% in A and C, and 75% in L. Age at presentation was 7.7 - 9.9 years younger than in the non smokers. Interestingly, non-smokers in groups C and L were usually diabetic. Although specific physical findings are not given, A patients had ischemic symptoms an average of 4.3 years, and the duration of symptoms in C and L was significantly shorter— 2.7 and 1.4 years respectively.

Because arteriographic studies are expensive and invasive, it has not thus far been feasible to routinely follow the progression of arteriosclerosis obliterans of the lower extremity with this accurate visual tool. Limited studies have presented patients who had repeat studies following bypass surgery or when clinical indications reemerged (20). However, Kuthan et al. (44) performed repeat femoral angiography and aortography on 1196 extremities of 705 male patients. Intermittent claudication was the sole complaint in 89% of these patients, who then had follow up studies at an average of 2.5 years after initial evaluation. This was an unprecedented look at the natural history of ASO patterns, in that most patients were not candidates for, nor previous recipients of revascularization. It was found that the rate of new occlusions was 31%, and new stenoses (defined as 1 - 99% obliteration of the lumen) 21%. The sum, 52%, was termed the incidence rate of progression. Changes such as dilatations, tortuosities, retractions of plaque, and thrombi, were regarded as minimal and discounted. the progression rate was 35% in those under 50 years old, and 61% above 50 years. The progression rate in overt diabetics was 65%, but no age specificities are given. Progression rates were analyzed for 14 initial pattern types and then for isolated cognate arteries. It was found that arteries displaying stenosis on initial study had the highest rate of progression. Frank occlusion on initial evaluation had little effect on progression, however the occlusion usually lengthened proximally from the original site. As an isolated arterial segment, the proximal 2/3 of the SFA had the highest rate of progressive disease, perhaps because as has been noted elsewhere (32) the distal SFA (at the adductor canal) is the most common occlusion and acts as a nidus for proximal disease. Numerically, the most common presenting patterns were frank SFA occlusion with or without trifurcation involvement, but these had among the lowest rates of progression. Among the highest rates of progression were patterns with stenoses of the femoral vessels and variable states of the trifurcation. Isolated tibial - peroneal stenoses had the 4th highest rate of progression, whereas isolated tibial - peroneal occlusions had the lowest of all patterns. It is tempting to extrapolate from this that possibly the monosegmental femoral occlusions commonly seen in the nondiabetic exert a hemodynamically protective effect on the distal runoff.

As isolated arterial segments independent of total pattern, the profunda, popliteal and trifurcation vessels had the lowest rates of new stenoses and occlusions, but one of the major drawbacks of this impressive study was that only 39 diabetics participated. In addition, the specific patterns of the diabetic patients and the 75 who presented with rest pain and/or tissue loss are not specified.

Unfortunately there is no further follow up nor information given as to therapeutic fates of these patients - i.e. whether certain angiographic patterns early in the disease process offer greater prognostic and management direction to the vascular surgeon.

B. Studies Distal to the Ankle and a Note on the Role of Microangiopathy

As the techniques of revascularization and limb salvage have improved over the past two decades, more distal bypass anastamoses to the level of the mid-calf and ankle are beginning to enter the realm of the routine (59,29). Hence assessment of the trifurcation and its final ramifications in the vessels of the foot is important for ultimate salvageability of an ischemic and/or gangrenous distal lèg and foot (37).

Limited studies have been performed comparing patterns of ASO distal to the ankle in diabetics and nondiabetics; the major fault of these comparisons is that they were performed at the end stage of disease, amputation. Edwards (22) performed arteriographic injections in 4 diabetic and 9 nondiabetic specimens. These were compared with the limbs of 2 young persons who underwent amputation for nonvasvular reasons. He found no particular difference between the degree of ASO in the foot arteries and arterioles of nondiabetics and diabetics. It was found that the arterioles of the calcaneal area, the dorsal plantar arch, and the medial artery of the hallux and lateral artery of the 5th digit were commonly affected.

Ferrier (25) combined arteriographic, plain x-ray, and histopathologic technique in analyzing 20 lower leg amputation specimines, 10 of which were from diabetic patients. Ferrier found no significant difference between the degree of obstruction of the tibial vessels in the two groups. The posterior tibial was most frequently obstructed, the peroneal least often. As per Edwards, no significant difference was found between the pedal vessels in the two groups. The major difference was the more extensive medial calcification in the diabetic arteries, which was found to increase as the size of the vessel lumen decreased, and could thus play a role in functional obstruction, especially of the metatarsal and digital arteries.

In a similar but non-roentgenographic study, Conrad (16) made acrylic casts of the vascular lumens of ten diabetic and ten nondiabetic lower limbs amputated for gangrene. There was no difference in the average age (65) of the amputees. There was also no significant difference between the average systolic blood pressures (145 mmHg), digital blood pressures (14 -18 mmHg), and digital blood flow (.010-.012 ml/min/5ml). Normally there is no pressure drop between brachial and digital readings; in all limbs the pressure drop was around 130 mmHG.

There was a somewhat greater amount of calf vessel occlusion in the diabetics, but overall extent of cognate vessel obstuction was about the same in both groups. The symptoms of the nondiabetics prior to admission revealed a history of chronic disease with a superimposed acute event prompting amputation, whereas the diabetics had no such acute events. This has been noted in other studies as well (20,41). The pre-operative arteriograms in these patients revealed no significant differences in iliac (20%) nor femoropopliteal (60%) involvement. Small vessels (10-250 microns) were examined in muscle and skin and no difference found in the extent of occlusion in the two groups. If the diabetic predisposition to ulceration and gangrene were to be explained on the basis of microangiopathy, then necrosis of tissue in the diabetic extremity should have occured in the presence of higher digital blood flow.

Diabetic microangiopathy is well beyond the visual and technical limits of the vascular surgeon or angiographer, and beyond the 'anatomic' scope of this thesis. However in concluding this review of leg vessel ASC and its comparative distribution in diabetics and nondiabetics, some comment on the practical implications of this controversial topic is warranted.

Microangiopathy, and its role in the vascular disease of the diabetic, especially the adult-onset diabetic, is a topic which has been debated for the past 25 years without successful resolution. In 1959 Blumenthal et al. (10) described non-atheromatous endothelial proliferation and deposition of P.A.S. positive material in the vasa vasorum, peri-adventitial vessels of cognate arteries, as well as arterioles of nerve, muscle and skin in 72% of the amputation specimens of diabetics, and only 8% of nondiabetics. The authors concluded that this type of small vessel disease could account for diabetic neuropathy and the patchy distribution of diabetic gangrene. Unfortunately these findings did not stand the test of reproducibility (14,57). Strandness et al. (70), used the same techniques as Blumenthal and could not find any differences in the arterioles of 15 diabetic and 19 nondiabetic amputation specimens; at the more proximal level of the trifurcation he found 81% involvement of the calf vessels in the diabetic and 57% in the nondiabetic. Besides the pathologic evidence, Strandness et al. showed that basal blood flow and pulse characteristrics in the limbs of both groups were not different, but there was a degeneration of peripheral vasomotor (sympathetic) tone in 27% of his diabetic group.

Barner et al. (3) similarly measured basal and peak flow in femoropopliteal bypass grafts (all autogenous saphenous vein) in nondiabetic and diabetic extremities treated with papaverine. Peak flow was greater in the nondiabetic, but when the better status of the trifurcation vessels in nondiabetics was accounted for and negated statistically, there was no significant difference between the two groups, and thus demonstrated physiologically no specific arteriolo-capillary affectation in the diabetic.

More recent editorials and reviews have not clarified the role of capillary basement membrane thickening (BMT) in diabetic leg-vessel disease. It is acknowledged that BMT is a normal consequence of aging and a lesion which is segmental in nondiabetics and diabetics (75). Interestingly BMT is less (by measured width) in pectoral muscle than in abdominal muscle, less in abdominal muscle than quadriceps femoris, and less in quadriceps femoris muscle than in the calf muscles; this is true in the nondiabetic, but more pronounced in the nondiabetic. According to Vracko(75) the amount of BMT is not related to duration nor control of the diabetic state as was once thought, and is also seen in many other pathologic states, e.g. gout, SLE, myxedema, CHF, etc., and in different organs from one individual the range of thicknesses may vary greatly. Williamson and Kilo (78) cite some interesting possible etiologies including hormonal (gonadotropins), direct effect of hyperglycemia, rheologic disturbances and increased venous hydrostatic pressure. Vracko (75) and McMillan (52) further propound the view that diabetic endothelium is more sensitive to injury and that accellerated cell renewal may lead to greater BMT. However, it is known that hypertension, a known aggravator of vascular disease in diabetics and non diabetics, is not always present in these patients and that it is an arterial phenomenon besides.

At this time, there is no conclusive evidence that BMT interferes with vascular function per se, especially nutrient permeability or leukocyte migration. In fact the

BM of diabetics has been found to be abnormally leaky (2,14,79). Barner makes the impassioned argument (4) that the diabetic microangiopathy of the kidney, retina, heart etc. are systemic effects of the disease which are ascribed too much importance when dealing with leg vessel of adult-onset diabetics. Indeed,the continually improving (29) and more comparable results of bypass/salvage procedures (69, 74) in diabetics and nondiabetics should not preclude aggressive attempts at arterial surgery when clinically warranted and angiographically/surgically feasible (37,74) Since much of the work comparing arteriographic patterns of disease still quoted in current references (1) is from a different era in the treatment of both arteriosclerosis obliterans and diabetes and based on selected patient groups this study will attempt to reexamine and update some of questions regarding the distribution and treatment of leg vessel disease in diabetic and nondiabetic patients in light of more current medical, radiographic (37) and surgical capabilities.

III. MATERIALS AND METHODS

107 patients who underwent femoral angiography or translumbar aortography at Yale-New Haven Hospital between July 2, 1982 and June 3, 1983 were studied. Patients who had undergone these procedures for evaluation of leg trauma, for evaluation of acute embolic phenomena as a result of an unrelated procedure, etc. were not included in this study. Eleven nondiabetic and 10 diabetic patients were excluded because they had had previous aortic or leg artery revascularization procedures.

This left 34 nondiabetic patients and 28 diabetic patients with chronic ASO undergoing lower extremity angiography (for the first time) to evaluate their ischemic symptoms. These arteriograms were analyzed (based on the report) for patency, plaques (implying moderate disease of an arterial segment), stenoses (implying more severe change of the lumen), and frank obstruction of the following arterial segments:

1. Distal aorta
2. Common iliacs
3. Internal iliacs
4. External iliacs
5. Profunda Femoris (PFA)
6. Superficial Femoral (SFA)- proximal
7. SFA- distal
8. Popliteal- proximal
9. Popliteal- distal

Runoff of the trifurcation vessels was assessed using the simple three pattern grading system of Taylor (71) and Stipa and Wheelock (68) but with some modifications:

Grade 1 (good)- 2 or 3 continuous vessels extending to the ankle and crossing it to supply the foot

Grade 2 (fair)- 1 continuous anterior or posterior tibial artery supplying the foot -OR- 1 continuous peroneal artery reconstituting a diseased tibial vessel which then crosses the ankle to supply the foot

Grade 3 (poor)- All 3 vessels occluded at some point above the ankle but ith reconstitution of arterial supply to the foot

Grade 4 (absent)- All 3 vessels occluded with no demonstrable runoff to the foot

Based on the formula and tables presented in Colton (15), the clinical presentations, general disease patterns, and disease of arterial segements and trifurcation was subjected to chi-square analysis using the proportions of observed and expected results.

The medical records of these patients were examined for the following:

1. Age

2. Sex

3. Race

4. Presenting symptoms, with emphasis on presence or abscence of ulceration/ gangrene, history of rest pain, claudication

5. In the presence of tissue breakdown, evidence of infection based on notation of cellulitis or abscess and consequent treatment with local care/ antibiotics, etc.

6. Smoking history

7. Hypertension - History was considered positive if documented in the chart and currently treated

8. If diabetic- Duration of known disease (where noted), and current therapy

9. Treatment and fate of the initially affected limb(s) per progress/clinic note in chart as of December 1, 1983

IV. RESULTS

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Ages of the 63 patients are presented below with their distributions by decade:

(Table 1)

AGE	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
40-49	2	7.1	2	5.7
50-59	6	21.4	11	31.4
60-69	9	32.2	7	20.0
70-79	11	39.3	13	37.1
80-89	0	0.0	1	2.9
90-99	0	0.0	1	2.9
	28	100.0	35	100.0
Average Age	64.54		64.77	

Of these patients there were 8 female diabetics and 11 nondiabetics. There were only 6 black patients, 1 male and 2 female diabetics and 2 male and 1 female nondiabetic.

57% of the diabetics and 80% of the nondiabetics had an antecedent history of intermittent claudicaticn, however upon presentation for angiography, the chief complaints were as follows:

CLINICAL PRESENTATION (Table 2)

Symptom	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %	
claudication only	4	14.3	13	37.2	
rest pain only	4	14.3	17	20.0	
rest pain with ulcers/gangrene	11	39.3	9	25.7	
ulcers/gangrene only	9	32.1	6	17.1	
	28	100.0	35	100.0	(p<.07, close to signif.)

Of the latter two groups in table 2, 11 of the diabetic patients (39.3%) a and 6 of the nondiabetic patients (17.1%) were treated presumptively for an infected foot.

82.1% of the diabetic patients had a previous history of cigarette smoking ranging from 10 - 113 pack-years; 64.3 % were still smoking at the time of admission. 85% of the nondiabetics had a smoking history ranging from 10 - 113 pack-years; of these, 68.6% were still smoking.

64.3% of the diabetics and 42.9% of the nondiabetics were being treated for hypertension. Of the diabetic patients, all were of the adult-onset type; 14 were being treated with insulin, 9 with oral hypoglycemics, and 5 with diet. Two of the diet-treated group were patients who were diagnosed as diabetic on admission for angiography. Duration of disease/current therapy was not always noted in the patient's chart, however the insulin-treated group ranged from 6-27 years with an average of 17 years, the hypoglycemic group ranged from 5-25 years with an average of

10.6 years, and the diet treated had their disease usually less than 5 years.

Based on the arteriographic findings, the patients were classified in 6 basic patterns of disease (Table 3). Arteriosclerosis obliterans is a systemic disease which affects most segments of the arterial tree; for instance, the majority of patients had some degree of compromise of the trifurcation , but if their runoff was graded 1 or 2 (good or fair) in both extremities, then "tibioperoneal" was not appended to their disease pattern. Likewise, qualification for a more proximal named pattern was based on what was described as stenosed or occluded by the angiographer. Plaques and ectasias that were considered minimal by them did not figure in the naming of patterns. In the nondiabetic group, one patient who had femoropopliteal disease did not have her more proximal vasculature mentioned in the official report. For this reason the tables concerned with distal aorta (table 4) to the PFA (table 8) cover 68 limbs in 34 nondiabetic patients; the rest cover 70 limbs in 35 patients.

PATTERN OF DISEASE (Table 3)

Distribution	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %	
1. Aortoiliac	1	3.6	5	14.3	
2. Femoropopliteal	4	14.3	7	20.0	
3. Tibioperoneal	5	17.9	2	5.7	
4. Aortoiliac + femoropopliteal	9	32.0	10	28.6	
5. Femoropopliteal + tibioperoneal;	7	25.0	6	17.1	
6. Aortoiliac + femoropopliteal + tibioperoneal	2	7.2	5	14.3	
	28	100.0	35	100.0	(p>.10, not signif.)

Arteriosclerosis Obliterans in Individual Arterial Segments

DISTAL AORTA (Table 4)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %	
patent	16	57.2	12	35.3	
plaque	9	32.1	18	52.9	
stenoses	3	10.7	4	11.8	
	28	100.0	34	100.0	(p<.10, not signif.)

COMMON ILIAC ARTERIES (Table 5)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %	
patent	30	53.6	26	38.2	
plaque	8	14.3	22	32.4	
stenosed	18	32.1	16	23.5	
occluded	0	0.0	4	5.9	
	56	100.0	68	100.0	(p<.05, significant)

EXTERNAL ILIAC ARTERIES (Table 6)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	43	76.8	45	38.2
plaque	0	0.0	8	11.8
stenosed	11	19.6	12	17.6
occluded	2	3.6	3	4.4
	56	100.0	68	100.0

(p<.07, close to signif.)

INTERNAL ILIAC ARTERIES (Table 7)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	44	78.6	39	57.4
plaque	2	3.6	11	14.7
stenosed	3	5.4	12	17.6
occluded	7	12.4	6	10.3
	56	100.0	68	100.0

(p<.01, significant)

PROFUNDA FÈMORIS ARTERY [PFA] (Table 8)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	46	82.1	54	79.4
plaque	0	0.0	5	7.4
stenosed	8	14.3	8	11.8
occluded	2	3.6	1	1.4
	56	100.0	68	100.0

(p>.1, not signif.)

SUPERFICIAL FEMORAL ARTERY [SFA] PROXIMAL (Table 9)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	20	35.8	32	45.7
plaque	11	19.6	10	14.3
stenosed	11	19.6	4	5.7
occluded	14	25.0	24	34.3
	56	100.0	70	100.0

(p<.07, close to signif.)

SUPERFICIAL FEMORAL ARTERY [SFA] DISTAL (TABLE 10)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	18	32.1	27	38.6
plaque	14	25.0	10	14.3
stenosed	13	23.2	11	15.7
occluded	11	19.7	22	31.4
	56	100.0	70	100.0

($p>.1$, not signif.)

POPLITEAL ARTERY [Proximal] (Table 11)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	35	62.5	50	71.4
plaque	11	19.6	4	5.7
stenosed	9	16.1	10	14.3
occluded	1	1.8	6	8.6
	56	100.0	70	100.0

($p<.05$, significant)

POPLITEAL ARTERY [Distal] (Table 12)

Extent	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %
patent	27	48.2	47	67.1
plaque	11	19.6	4	5.8
stenosed	10	17.9	12	17.1
occluded	8	14.3	7	10.0
	56	100.0	70	100.0

($p<.07$, close to signif.)

The trifurcation vessels are analyzed by overall grade and then compared in diabetic and nondiabetic limbs for statistical difference. The presence of ulcers/gangrene is then correlated with the grade of runoff in an affected limb (22 diabetic and 18 nondiabetic limbs overall had evidence of tissue breakdown):

TRIFURCATION VESSELS-GRADE of RUNOFF (Table 13)

GRADE	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %	
1.Good	17	30.4	21	30.0	
2.Fair	22	39.2	35	50.0	
3.Poor	14	25.0	13	18.6	
4.Absent	3	5.3	1	1.4	(p>.10,
	56	100.0	70	100.0	not signif.)

LIMBS WITH ULCERS/GANGRENE OF THE FEET-
UNDERLYING GRADE OF TRIFURCATION (Table 14)

GRADE	Diabetic #	Diabetic %	Nondiabetic #	Nondiabetic %	
1.Good	5	22.7	3	16.7	
2.Fair	9	40.9	6	33.3	
3.Poor	6	21.4	9	50.0	
4.Absent	2	9.0	0	0.0	(p>.10
	22		18		not signif.)

The therapeutic outcomes of these patients will be presented in the discussion.

V. DISCUSSION

Susceptibility to ASO and its complications are raised in diabetes mellitus (65). Despite advances in the care of these patients, these risks have not been significantly lowered (81), although the diabetic patient may be living free of complications for a longer period of time than before. Conversely, there has been a general clinical impression that ASO, though slower in its progression, is now recognized in younger nondiabetics (39,61). In this study, the average age of patients in these two groups is the same, however small differences among the averages in the patterns emerged. For instance, in the nondiabetics the aortoiliac group of patients average 57.2 years (there was only 1 diabetic in this group), femoropopliteal-tibioperoneal group average 60.7 years (9 years younger than the diabetics in that group), aortoiliacfemoropopliteal average 59.7 years (almost five years younger than the diabetics in that group).

There are 9 female diabetic patients (32.1%) and 10 female nondiabetics (29%), but due to the limited numbers of patients studied it is not possible to comment further on the male:female ratio.

It is interesting that greater numbers of nondiabetics reported an initial history of intermittent claudication (table 2), which has also been reported in other series

(39,9,20). Schadt (61) reported that nondiabetics have claudication an average of one year longer than their diabetic counterparts, who then progress more rapidly to rest pain or necrosis. Although the time course of the antecedent symptoms in these patients was not explored, it is clear that they present for angiography at a more advanced phase of their ischemic symptoms, but roughly at the same age as nondiabetics. It is appropriate to consider the role that neuropathy could play in the subjective complaints of these patients. Only one diabetic, a 65 year old female patient, has a documented history of peripheral sensory neuropathy, and presented with ASO in an aortoiliac-femoropopliteal distribution but fair runoff to the feet. There are 4 other patients with symptoms such as cold and paresthetic legs/ feet noted in addition to their dysesthesias at rest. In such patients it is difficult to sort out the neuropathic from ischemic complaints, although in the earlier stages of ASO this might be accomplished by testing exercise tolerance. Neuropathy that produces hypesthesias is probably important not only from the familiar scenario of painless trauma, but also as it interacts and alters the symptoms of ischemia. Joint changes and neurotropic ulceration (mal perforans) are seen in the presence of intact peripheral pulses in about 15% of patients with "diabetic feet" (23), but usually the diabetic leg presents with a spectrum of vascular compromise superimposed on some sensory, autonomic and motor impairment as well. It is noteworthy that neuropathy with a purely ischemic basis is not unknown in the nondiabetic (81). This is usually not a hypesthetic phenomenon as in diabetics, but rather part of the etiology of rest pain. Steer et al. (68) notes that ulceration with rest pain is the worst prognostic sign for limb salvage and mortality. Although our diabetic patients had more of this type of presentation than any other, Steer found this to be statistically independent of diabetic status.

With regard to risk factors in these patients, cigarette smoking is similarly pervasive as in other studies (6,14) but not more prevalent in any one particular pattern of disease. A considerable number of both diabetics and nondiabetics claimed to have given up this habit at some time before this admission. Intermittent claudication is twice as great in smokers as nonsmokers, and the risk tends to increase with the intensity of the habit (14). In addition to shifting the oxygen dissociation curve, smoking has been shown to increase blood lipids and platelet adhesion (19). Smoking (probably via nicotine) decreases reactive hyperemia and cutaneous blood flow and so enhances vasomotor tone via the sympathetic nervous system. Juergens et al. (39) showed that continued smoking in patients with leg vessel disease led to more amputations than in those who stopped. Other studies have demonstrated the deleterious effects of continued smoking on the patency and success of revasculariztion procedures (55).

Treated hypertension is 1.5 times more prevalent in the diabetic group. Because of observer variability in these records, it was not possible to ascertain the exact duration of the condition. The high proportion of hypertensive patients in this study are notable because of the lower numbers of hypertensives that are seen in prospective studies (80,81,70) which follow the natural history and progression of leg vessel disease; in these studies there are proportionately more hypertensives among the nondiabetics. This again probably reflects on the more rapid systemic progression of cardiovascular disease in the diabetic.

The patients are classified into 6 patterns of disease (table 3). Nondiabetics have a greater incidence of disease involving the aortoiliac segment alone and in combination with femoropopliteal-tibioperoneal disease. Diabetics have more tibioperoneal disease, whether isolated or combined with femoropopliteal disease. Femoropopliteal disease by itself is somewhat higher in the nondiabetic. Some of these findings concur with the work of Haimovici (see page 12), however, none of the present findings on these basic patterns of occlusions/stenoses are statistically significant.

To characterize in greater detail the arterial lesions of these patients, individual segments (except for the common femoral, due to variability in reporting) are characterized in the manner of Kuthan et al. (44). The disparity of ASO distribution between diabetic and nondiabetic are mostly seen above the inguinal ligament. Nondiabetics have greater involvement at all levels of the aortoiliac segment, and this is significant at the common iliac and internal iliac arteries, and is close to significance at the external iliac arteries (tables 4-7).

Unlike the later findings of Haimovici (30) there is very similar involvement of the profunda femoris in both groups, with somewhat more serious involvement of this vessel in diabetics; again however, the observations were not in the range of significant difference (table 8)

The proximal SFA (table 9) has overall less disease in nondiabetics, but more frank occlusions; the differences are close to statistical significance. Of note is that in diabetics and nondiabetics this vessel has greater numbers of occlusions than any other. The distal SFA (table 10), is the second most occluded vessel overall in both groups, but the lowest in overall patency; the state of this segment is very similar in both groups. Although more occlusions are seen at the proximal popliteal (table 11) in the nondiabetic, more overall disease is seen in the diabetic. The distal segement (table 12) also displays more overall disease in the diabetic, but unlike the proximal popliteal this is not quite statistically significant.

Although grading of the trifurcation vessels does not pinpoint individual lesions of the tibial-peroneal arteries, it does provide an objective and standard assessment of the runoff below the knee (table 13). Diabetics do have more limbs in the "poor" and "absent" categories, but reflecting the anatomic and statistical continuity with the distal popliteal, the differences in the condition of the trifurcation are not significant. When analyzed for the presence of soft tissue necrosis (table 14), the diabetics have a greater incidence of ulcers/gangrene in the presence of a "good" or "fair" runoff than nondiabetics, but this was not statistically significant. In the presence of presumptive infection , however, the diabetic group has much less compromise of distal as well as proximal flow. Of 12 limbs in 11 diabetic patients described/treated for infection (cellulitis, abscess, etc.), 3 had "good" runoff, 5 "fair", 3 "poor", and 1 "absent". In the non diabetics, 5 of the 7 infected feet had "poor" runoff , and only 2 had "fair" runoff. Whereas most of these diabetic patients have associated patterns of femoropopliteal disease, the nondiabetics with presumptive infections have worse runoff with associated disease of aortoiliac and femoropopliteal segments combined. Of these patients with infection, 2 major and 1 minor amputation were performed in the nondiabetics, and 4 major and 6 minor amputations were performed in the diabetic group.

It would seem from the above that diabetics are not so much distinguished by the more distal distribution of their ASO, as their inability to resolve infection and heal ulceration in the presence of outwardly (i.e. angiographically) less severe vascular compromise than their nondiabetic peers. This translates therapeutically into a greater number of minor amputations which are performed in the presence of adequate runoff or a functioning bypass graft (41,45).

Overall, 5 nondiabetic patients (14.3%) underwent major amputations. Two of these were primary above-knee amputations in patients with acute exacerbation of rest pain as a result of thrombus. Three resulted from early failure (1-3 months) of arterial surgery. Four of these patients had diffuse, multilevel disease (aortoiliac-femoropliteal-tibioperoneal pattern). Seven diabetic patients (25%) had a major amputation. Two were primary procedures for refractory, nonreconstructible ulcerated limbs. Five were secondary to unsuccesful revascularization procedures which failed between 1 and 2 months. Similar percentages of diabetic (21.4) and nondiabetic (25.8) patients either required no surgery and were to to be followed as out-patients, or responded to conservative debridement and antibiosis.

Angioplasty was used as the primary treatment of 2 diabetic patients, 1 with aortoiliac disease and one with an SFA stenosis. The former case resulted in an above-knee amputation; despite increased flow to the patient's foot, her ulcers did not heal. The latter case yielded equivocal results, but did result in limb salvage in the presence of aortoiliac-femoropopliteal-tibioperoneal disease. Three nondiabetic patients underwent iliac angioplasty for aortoiliac (1 patient) and aortiliac-femoropopliteal (2 patients). Two other nondiabetics had a profundoplasty (PFA angioplasty) as intraoperative adjuncts to endarterectomy or bypass. There were no profundoplastys performed in the diabetic patients. It has been seen in other surgical series (34) that the incidence of severe disease of the PFA in diabetics approached only 5% (again in contrast to Haimovici) but that profundoplasty was of little value in improving the collateral circulation in these patients anyway. All of the nondiabetic patients had good results with relief of symptoms. Spence et al. (64) found better long term patency of the iliac arteries in diabetic patients undergoing transluminal angioplasty, but better patency of the femoral arteries in nondiabetics; runoff below the popliteal had less effect on ultimate salvage of the limb than anticipated.

Bypass grafting showed similar results in diabetics and nondiabetics. Four nondiabetic patients had aorto-femoral bifurcation grafts for aortoiliac (1 patient) and aortoiliac-femoropopliteal (3 patients) disease. Three diabetic patients had bifurcation grafts for aortoiliac-femoropopliteal disease. There were good results in all of these patients. Two nondiabetics had aortobifemoral grafts and femoropopliteal bypass grafts as treatment for their diffuse aortoiliac-femoropopliteal-tibioperoneal disease, but both cases resulted in below-knee amputation. Brewster et al. found that soft tissue necrosis and poor runoff (which these 2 patients had) are strong predictors of failure when proximal reconstruction is the only feasible treatment for multilevel disease (11).

Nondiabetics had 10 femoropopliteal bypasses and 2 bypasses to the tibial arteries as single procedures. The diabetics accounted for 12 femoropopliteal bypasses and 2 tibial bypass grafts. There were two early graft failures in the diabetic group which resulted in below-knee amputations; the tibial bypasses have remained patent. With longer follow- up now available, many studies (29,34,59) are finding comparable results in diabetic and nondiabetic patients who undergo distal bypass for tibioperoneal disease with or without femoropopliteal involvement. As mentioned earlier, 6 diabetic patients underwent minor amputations (toes, transmetatarsal) to insure successful bypass as opposed to one nondiabetic. Little et al. (50) has reported that 75% of patients with initial conservative amputations eventually lose the affected limb. In that study, the presence of diabetes had nc effect on outcome.

Eight lumbar sympathectomies were performed on 7 nondiabetic patients and 1 diabetic patient, with disappointing results. Only 1 nondiabetic had improvement of bilateral malleolar ulcerations, but skin grafting was required. Another nondiabetic had equivocal results, one had a below-knee amputation, and one expired of sepsis post-operatively. Sympathectomy was the only surgery performed in these four cases, and in the diabetic patient, who shortly afterwards required a below knee amputation as well. Three nondiabetics underwent sympathectomies in addtion to femoropoliteal bypasses. Only 1 patient had a good result; the other had equivocal results and the third patient had poor results but refused amputation. For the past 50 years sympathectomy has been performed for end stage arterial disease when bypass is not feasible. There is no well defined method of determining preoperatively who will respond favorably, even when an equivalent pharmacologic block is used prior to actual surgery. Although the purpose of this surgery is ostensibly to dilate collateral channels, circulatory shunts do occur which may actually lead to infarcts of the toes or distal foot. DaValle et al. (17) recently reported that at 5 years post-op, only 19.1% of diabetics and 51.6% of nondiabetics had avoided amputation.

Interestingly, the success rates were the same for diabetics and nondiabetics under 65 years old. DaValle et al. attribute the worse overall results in diabetics to their propensity to infection and the "autosympathectomy" of diabetic neuropathy. This group performed electron microscope quantitation of nerve endings on epineural arterioles of the sural nerve, and found them reduced in number in diabetics, but without further reduction post-sympathectomy.

Two of the patients in the diabetic group were diagnosed as such on admission for angiographic evaluation of their leg vessel disease. Both patients were males in their early 70's. One patient had multilevel ASO in the presence of multilevel disease but was not in need of surgery. The other patient had an infected nonhealing ulcer secondary to trauma, and required femoropopliteal bypass grafting and a transmetatarsal amputation. The studies of Schadt et al. (61) and Bartels and Rullo (5) have found that between 15-20% of unselected patients with signs of arterial insufficiency are then newly diagnosed as diabetic. Glucose tolerance is known to diminish with age, but Kingsbury (42) correlated a greater number of leg vessel occlusions on angiogram with an increased degree of glucose intolerance in 338 male patients;and found that the occlusive/biochemical spectrum was unrelated to age.

VI. CONCLUSION

Serial arteriography remains the most precise method for evaluating the leg vessels in ASO. The newer D.I.V.A. (digital intravenous arteriography) techniques hold promise for a simpler less risk-prone method of visualization. At this time however, D.I.V.A. studies are not applicable because of present limitations in view field and contrast enhancement (31,53). Digital technique applied to the standard arterial injection, with the adjunct of reactive hyperemia for greater visualization of the distal calf and pedal arches, is proving more patients reconstructable, when their severe ASO might have warranted amputation in the recent past (37,73). Unfortunately, this has not eliminated the risk or expense of the standard procedure and like D.I.V.A. is not applicable for routine, precise follow-up before surgery is indicated.

The persistent dilemna of vascular reconstruction is the interplay and interface of anatomy and physiology in the lesions of ASO. Much interest has now turned from the precise anatomic delineation of obstruction to the hemodynamic and functional significance of occlusive disease as determined by noninvasive methods (53,67). The obvious advantages are their ease, safety and follow up capabilities. However, these methods can only give rough estimates of obstructions/stenoses, pressure drops, etc. and can by no means predict the course of the disease nor the success of surgical intervention. Using the methods of Carter (6,56,71) who compared ankle/brachial systolic pressure ratios (which should normally be 1 or greater), rough indices have been established for claudication (.5-.7) and ulceration (.4 or less) etc. These standards however do not guarantee adequate perfusion of the distal foot, for instance. Many of the prospective studies now in progress (6,56,80,81) use noninvasive testing for follow-up and comparison of ASO in the leg vesels of diabetics and nondiabetics. Bendick et al. (9) studied 294 diabetic patients and found that 36% had ASO initially, and that 34% showed new disease or serious progression at 2 years. The strongest indicator for progression was preexisting disease,(echoing Kuthan's radiologic study done predominantly with nondiabetics (44)), and bore little relation to diabetic "control" etc. Bendick et al. found that runoff distal to the popliteal could be expected to be "good" in half of the patients, and the study goes so far as to recommend earlier and more aggressive surgical treatment of lower extremity ASO in the diabetic. The role of noninvasive studies in the evaluation of diabetic ASO is still controversial. Because of the greater degree of medial calcification and resultant noncompressibility of diabetic arteries, the accuracy of pressure/Doppler evaluation is regarded with some doubt (12,43). However, based on the findings of this study, it would appear that the major clinical difference between diabetics and nondiabetics is that diabetics present for angiography (hence revascularization) at a more advanced stage of their ischemic symptoms. This corroborates the rapid progression noted by Bendick et al. and is secondary probably to impaired healing capabilities and superimposed neuropathies. Anatomically, these patients differ mostly in that nondiabetics have statistically greater involvement of the aortoiliac vessels; diabetics showed no monopoly on worse runoff below the popliteals. It was impressive that diabetics had more severe tissue necrosis in the presence of somewhat better vascularity. Since both groups of patients fare similarly well with bypass grafts, I would tend to conclude that earlier intervention in diabetics could angiographically "arrest" ASO at a more reconstructible stage, and that resultant surgery would allay the larger numbers of major and perhaps even minor amputations in these patients. Studies more specifically addressing the fate of the diabetic claudicator would be helpful.

Thirty years ago, Bell (7,8) defined the prevalence of arteriosclerotic gangrene in diabetics and nondiabetics in a large autopsy series covering the years 1911 through 1955. He found that over age 40, gangrene is 50 times more common in diabetic males and 71 times more prevalent in diabetic females than nondiabetics. A disparity persists in the amount of diabetics who undergo amputation today (34), but much has changed since Bell's era, when up to 46% of patients with gangrene died as a direct result of this tissue necrosis. Though current studies may continue to quote Bell (49) few patients today die of their leg vessel disease. Many, up to 20% at 2 years after presentation for arterial surgery (14,19), will die of cardiovascular disease due to the systemic effects of ASO. It is therefore imperative that limb salvage in these patients continue to improve-- between 30-70% of patients who have had a major amputation never learn to use a prosthesis (40,68); this greatly reduces the quality of an already potentially reduced quantity of life. Likewise, the review of the literature represents the most 'recent' angiographic data on leg vessel disease patterns in diabetics and nondiabetics. Clearly radiography and surgery have improved in the ensuing decades (as partly reflected in an amputation rate in vascular patients that has fallen from 20% in the 1950's to about 9% today (27,34)) yet published data has been limited to the initial limited studies and continues to be quoted (1) with out the perceived need for larger reexamination of the variable and somewhat inconclusive results of the important original arteriographic studies.

New information regarding the effects of "diabetic control" and such parameters as blood rheology (40), collagen and hemaglobin glycosylation (65) ideal body weight (9), and capillary thickening (13,58), as well as the atherogenic effects of insulin (66), may yield the medical clues to the disproportion of ASO in the diabetic. In practical terms, these advances will probably have their most positive and productive applications to the juvenile-onset diabetic, who has less leg vessel disease (6,8) to begin with, probably as a result of the younger patients involved, and as an indirect result of their disease being recognized and 'controlled' at an earlier stage. Diabetic leg vessel disease remains predominantly an affliction of the adult onset diabetic, whose metabolic abnormality may exist occultly for years before it is recognized, and whose symptoms may be masked by disregard or a sedentary lifestyle.

Patients over the age of 60, particularly those with other systemic signs (e.g. EKG abnormalities, etc.) of arteriosclerosis and important risk factors (especially diabetes) should be subject to closer follow up and concern regarding the possible development of leg vessel disease. Earlier diagnosis and control of diabetes, hypertension, lipid abnormalities, etc. may yet prove to directly improve/reverse the prognosis of these patients. As contrast studies and surgery improve, however, perhaps these may be offered at an earlier time with greater assurances when conservative treatment appears unlikely to stem the progression of limb ischemia. Until such time, education of both the patient and physician remains and will remain the most important factor in limb salvage, regardless of the underlying vascular pathology. Delbridge et al. (18) in an elegant study show that diabetic control and neuropathy play little part in the emergence of foot ulcers in diabetics. Lack of patient education regarding diabetic complications, foot care, etc. was more strongly correlated with tissue breakdown than other parameters.

When speaking of the potentially grim outcome of leg vessel ASO, particularly in the diabetic, the words of Joslin retain remarkable currency and prescience:

> If the [patient] kept his feet as clean as his face, gangrene would seldom occur... If the beginning were as noisily ushered in as an attack of biliary or renal colic the results would be far different. Gangrene today is the result of procrastination on the part of the physician and patient. Surgery often receives, but seldom deserves, the blame...(18)

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